

REMARKS

The non-final Office Action of May 18, 2006 has been carefully considered. A listing of the pending claims is provided but no claim amendments are made.

Claim Rejections – 35 USC § 102

Claims 1-8, 21 and 23 are rejected under 35 U.S.C. § 102 as being anticipated by Kahne et al. (US 2002/018266 A1) (“Kahne”). This rejection is traversed.

Kahne is directed to kinetic assays, and in particular method to identify inhibitors by monitoring a change in the amount of product formed in a reaction. In contrast, the invention as currently claimed is based on a donor displacement assay. The Examiner admits as much on page 4 indicating that “Kahne does not teach performing a donor displacement assay . . .” This admission alone removes Kahne as an anticipatory reference. While it is true that compounds that displace substrates inhibit enzymatic reactions (leading to a decrease in product formed as judged in a kinetic assay), it is not true that kinetic assays and displacement assays are equivalent. The differences between a kinetic assay and a displacement assay, and additionally between the donor and acceptor substrates, are quite significant and are not interchangeable to those skilled in the art.

Displacement assays are biased towards compounds that bind to one particular site on the enzyme. In the displacement assay, no chemical bond forming or breaking reaction occurs, as in the cited reference (where one measures the amount of coupling product). Kinetic assays identify compounds that can bind to either of the substrate binding sites or to a completely different site on the enzyme; they can also identify compounds that inhibit promiscuously (e.g., by denaturing the enzyme rather than by binding to it specifically). Disclosure directed toward performing a kinetic assay does not teach one of ordinary skill in the art how to carry out a displacement assay. Measuring the amount of product formed in a reaction is not the same as measuring the amount of substrate bound to an enzyme. In fact, measuring the amount of substrate used up in a reaction (e.g., in a kinetic assay) is not the same as measuring the amount of substrate bound to an enzyme under conditions where no reaction occurs. In addition, kinetic assays also require precise timing and can be technically demanding, particularly if they involve

secondary enzymes to detect product, as a colorimetric assay does. Finally, kinetic assays are often subject to nonspecific inhibition by compound aggregates, which creates uncertainty of the results obtained.

In contrast, the current invention as claimed in Claims 1-11 and claim 21 recite an assay that utilizes a donor displacement assay. In addition to being straightforward, technically simple, and inexpensive, a donor displacement assay provides other advantages that make it particularly useful for the screening of compounds. For one example, because the assay is based on displacement of a ligand from the glycosyl donor binding site, a relatively high number of hits bind to a single region of the enzyme. As a result, the structural requirements for binding to that region of the enzyme emerge quickly from an analysis of the data. In contrast, kinetic assays yield compounds that operate by a number of different mechanisms, making structure-activity relationships more difficult to analyze. Additionally, the method provides fewer false positives related to compound aggregation in the displacement assay compared with a kinetic assay due to reduced sensitivity to artifacts related to compound aggregation. Finally, the donor displacement assay can be readily adapted to screen any glycosyltransferase, for example, in which at least one modifiable group on the nucleotide-sugar is solvent exposed. See Specification at page 11, lines 12-15.

Claim Rejections – 35 USC § 103

Claims 1-11 and 21-23 are rejected under 35 USC § 103(a) as being unpatentable over Kahne et al. (US 2002/018266 A1) in view of Helm et al. (2003). This rejection is traversed.

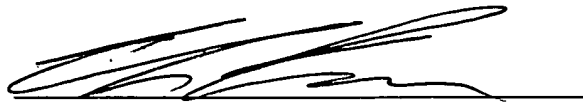
The Applicants submit that Kahne et al. is reference is not available under 35 USC § 103(a) as the reference is a publication in which the inventors are co-authors. In accordance with MPEP 2132.01, the Applicants submit declarations under 37 CFR 132 evidencing that Helm et al. 2003 describes one of the inventor's work only. Therefore, Helm et al. is not available as a reference under 35 USC § 102(a). Removal of the rejection is requested.

In view of the foregoing, Applicants submit that all pending claims are in condition for allowance and request that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. It is

believed that no fee is required. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

Dated: August 18, 2006

A handwritten signature in black ink, appearing to read 'Christopher S. Casieri', written over a horizontal line.

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